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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,697	09/27/2001	Tarlochan Singh Dhadialla	A01115A (RH-0036)	4412

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RheoGene, Inc.
2650 Eisenhower Avenue
Norristown, PA 19403

EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1649	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/965,697	DHADIALLA ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *5 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9-12 and 16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *011006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

Applicant is notified that the amendments put forth on 1/10/06, have been entered in full.

Claims 5 and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant's election with traverse of Group I, claims 1-4, 9-12, and 16-20 in the paper filed 4/7/05 is acknowledged, as set forth previously. It is noted that claims 6-8 also read on the elected group and will thus be examined in this Office action, as set forth previously.

Response to Amendment

Applicant is notified that any outstanding objection or rejection that is not expressly maintained in this Office action has been withdrawn in view of Applicant's amendments.

Maintained Rejections:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons:

Claims 16 recites the step of "defining a set of diversely modified ligands based on incremental pharmacophore element changes". This step renders the metes and bound unascertainable for the following reasons:

The specification nor the claims set forth what attributes are considered "defining" as it is used in the claims. The words "diversely", "modified" and "incremental", as used throughout the claim, are each relative words yet the specification nor the claims have provided no distinct teaching as to when the parameters of these words are exceeded, and thus the artisan could not be reasonably sure that he or she were practicing the claimed invention.

Applicant argues that art recognizes the terms used in the claims. This argument has been fully considered but not deemed persuasive. The terms diversely", "modified" and "incremental" are relative terms. Terms in the claims are to be given their ordinary English meanings. Since the metes and bounds of the claims cannot be determined, the claims are indefinite.

Claim 16 recites the step of "querying the receptor polypeptides" yet the claims do not specify what questions or inquiries are meant to be encompassed by the query.

Applicant argues that the phrase "querying the receptor polypeptides" is modified by the phrase "for gene modulation or ligand domain binding or both". Additionally, Applicant provides arguments regarding the definition of "gene modulation" and "binding to the ligand domain binding". This argument has been fully considered but not deemed persuasive. The specification does not set forth what steps are meant to be encompassed by querying the receptor polypeptides as this relates to "gene modulation". The specification does not define the term.

Claim 16e requires the step of determining the orthogonality of the receptor polypeptide/ligand combination to define a subset of ligands with diverse gene modulation properties. It is unclear what nexus there is, if any, between "determining the orthogonality of the receptor polypeptide/ligand combination" and "to define a subset of ligands with diverse gene modulation properties". It is unclear how the first accomplishes the second. The claims are therefore indefinite as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Applicant argues that "the orthogonality of the receptor polypeptide/ligand combination" is strictly defined by the specification at page 26. This argument has been fully considered but not deemed persuasive, as the definition of orthogonality was not an issue in the rejection. Applicant provides several figures in the discussion of the relationship between determining the orthogonality of the receptor polypeptide/ligand combination" and "diverse gene modulation properties". This argument has been fully considered but not deemed persuasive. The specification or claims must establish the bounds of the claim. As set forth above, it is unclear what applicant is claiming because of the presence of these two phrases. No step(s) are provided that establish the bounds of these phrases, thus the metes and bounds of the claim cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 4, 6-10, 12, 14-20 are rejected under 35 U.S.C. 102(b) as being anticipated by MORADOPOUR-D et al. Biol Chem 379(1189-1191)1998. At Col 2 of page 1189, MORADOPOUR-D et al., disclose a multiple inducible gene modulation system comprising a plurality of individually operable gene modulation systems wherein each individually operable gene modulation system comprises:

i) one or more polynucleotides encoding a receptor complex comprising:
A) a DNA binding domain,
B) a ligand binding domain,
C) a transactivation domain,
i.e. tTA or pVgEcR-RXR or both (as in claim 2),

ii) a ligand: i.e. tetracycline or muristerone A or both (as in claim 2)

iii) a polynucleotide comprising:
A) an exogenous polynucleotide:
B) a response element:
i.e. pUHC13 or pIND/lacZ or both (as in claim 2)

wherein the exogenous polynucleotide is operatively linked to the response element and binding of the response element in the presence of the ligand results in activation of the polynucleotide and each system is orthogonal (works independently) of the other systems (see the last paragraph of col 2 of page 1189). Furthermore, regarding claims 16-20, the procedures disclosed by MORADOPOUR-D et al. appear to read on the claims given their broadest reasonable interpretation, i.e. MORADOPOUR-D et al. defines a first set of set of polypeptide and ligands (tTA and tetracycline) a second set (pVgEcR-RXR and muristerone A) which are naturally occurring and chimeric, and expressed from cloned DNA, wherein the orthogonality of the two systems is assayed, see the last paragraph of col 2 of page 1189.

Applicant argues that MORADOPOUR teach a gene modulation system comprising a a ligand binding domain from one nuclear receptor and another ligand binding domain that is not a nuclear receptor. This argument has been fully considered but not deemed persuasive. Given the broadest reasonable interpretation of the term "nuclear receptor" as required by the claims, tTA would be considered a nuclear receptor, i.e. it binds its ligand intracellulariy, wherein it directly interacts with the DNA inside the nucleus of the cell to induce or suppress gene expression. This scheme is in contrast to non-nuclear receptors, e.g. GPCRs, that bind the ligand on the exterior of the cell and transmit the ligand binding signal from the cell membrane to the nucleus via other proteins and small molecule second messengers – as is well established in the art.

New Rejection:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over MORADOPOUR-D et al. Biol Chem 379(1189-1191)1998, as discussed above, in view of Hofmann-A et al., PNAS 93(5185-5190)1996.

Claims 3 and 11 require that the multiple inducible gene modulation system of claims 1 and 9, respectively, be comprised in a virus. As set forth above, MORADOPOUR-D et al.,

disclose a multiple inducible gene modulation system of claims 1 and 9, yet they do not disclose a virus comprising the system. In the last paragraph of MORADOPOUR-D et al, the difficulties of using the system is discussed with regard for the need of multiple transfections. Hofmann-A et al. teach that these difficulties can be overcome by developing a single cassette comprising the inducible gene modulation system with in a retrovirus, see column two of page 5185.

Therefore, one of ordinary skill in the art, at the time the invention was made, and with reasonable expectation of success, would be motivated to use a virus to express the gene modulation system of MORADOPOUR-D et al. The motivation to do so is provided by both MORADOPOUR-D et al, who admit to the problem of multiple transfections required to practice the inducible gene modulation system and by Hofmann-A et al. who teach that such problems can be overcome using a retrovirus.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

April 2, 2006